Lead poisoning from Contaminated Water Supplies, with special reference to the Significance of Punctate Basophilia.

Thesis for M.D. (Glasgow)

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Introduction.

It has been known for some considerable time that cases of lead poisoning from contaminated water supplies are continually occurring in different parts of Lancashire, but from the paucity of published cases, it does not appear to be realised how widespread this intoxication may be. Cooke (1) states that during the past few months several cases of lead poisoning have come under his notice, and he thinks that these are merely a tithe of the cases existing in Lancashire to-day. With this opinion I am in thorough agreement. Plumbism presents such a diversity of symptoms, especially in those cases with only a mild degree of poisoning, that unless one is on the look-out for it, many cases may be overlooked, and the patients classified as neurotic because of their never-ending visits to the consulting room. Sir Thomas Oliver (2) says, "I have not the slightest doubt that there are many cases of illness attended by obscure nervous symptoms of which no explanation can be given and which are illustrations of atypical plumbism. Patients thus suffering are seen and treated by medical men without the true nature of their malady being recognised." In my own practice, the occurrence of two or three cases of undoubted lead poisoning led to a systematic search for other cases, with the astonishing result that in one small area of the town alone, no less than

forty cases have been collected during the past five to six months. Many of these cases could not have been diagnosed as lead poisoning had not a special search been made for the condition, and every suspected case fully investigated until there was no doubt as to the diagnosis. Cases of typical lead poisoning have been known to occur in the town from time to time, but no previous attempt has been made to assess the amount of illness caused by the condition.

In this Thesis, the results of the investigation will be detailed, and special reference will be made to the significance of punctate basophilia in chronic plumbism.

Water Supply of Haslingden.

The town of Haslingden lies on the hill side at the lower end of the Pennine Chain in East Lancashire. The centre of the town lies about 850 feet above sea level, the older part being above this height, and the newer part below. In addition to being the higher part of the town, the older part contains the poorer area, and it is in this district that I have collected the present series of cases. The population of the town is about 17,500, and the principal industry is weaving.

The water supply of the town, supplied by the Bury and District Joint Water Board, is derived from two sources, Scout Moor and Clough Bottom Reservoirs. Scout Moor reservoir supplies the higher parts of the town, and Clough Bottom reservoir supplies the lower. Both reservoirs collect upper moorland waters, which are conducted from the gathering grounds to the reservoirs in open streams or channels, and from the reservoirs to the town by means of cast iron pipes. Those houses supplied from the public mains are connected by means of a gun-metal ferrule to the main with various lengths of service pipes, the latter being composed principally of

lead. In the older part of the town, some of these service pipes are known to have been in use for over 50 years. Not all the houses in the district are on the public supply, several receiving water from local streams or springs and from private reservoirs.

The Clough Bottom waters are filtered, no coagulant being used, while Scout Moor waters, supplying the higher parts of the town, receive no treatment whatever. Since this investigation is entirely confined to the water obtained from Scout Moor reservoir, it has not been thought necessary to give any analysis of the water from Clough Bottom reservoir.

Analysis of water in reservoir and in public mains.

In any enquiry into the purity of a water supply, analysis of water from the household taps does not give sufficient information to condemn the water. It is necessary to examine the water from the source of supply, from the reservoir, and from the public mains. Knowing that these analysis were carried out periodically by an analyst on behalf of the Bury and District Water Board, a letter was directed to the Board requesting permission to use the results already known. The analysis covering a period of two years were immediately made available, and include drinking water analysis, mineral analysis, and plumbo-solvency tests.

The following table gives the results of the drinking water analysis carried out in Septr. 1929 and in Septr. 1930. That analysed in 1929 was taken from the regulating well at the reservoir, where the water enters the mains, and that in 1930, from the mains in Haslingden.

Table I.

	Regulating well where water enters mains. (3/9/29).	From main in Haslingden. (3/9/30).
Appearance	Slightly opalescent	Bright and clear.
Suspended matter	Heavy traces	Nil.
Odour at 100 degrees F.	Slightly grassy.	Practically nil.
Colour in 2 ft. tube	Slightly peaty.	Slightly peaty.
Taste	Satisfactory.	-
	Parts per 100,000.	
Free and Saline Ammonia	0.0030	0.0032
Albuminoid Ammonia	0.0216	0.0080
Oxygen absorbed in 4 hours	0.0712	0.0891
Nitrogen as Nitrates	0.040	0.025
Nitrogen as Nitrites	Nil.	Nil.
Chlorine	1.21	0.93
Phosphates	Practically nil.	Nil.
Iron	0.010	0.034
Heavy metals and zinc.	Nil.	Nil.
Total dissolved solids.	10.0	7.6
Reaction to methyl-orange	Acid.	Acid.
Reaction to phenol-phthalein	Acid.	Acid.
pH value	4.3	About 4
Hardness (degrees) all permanent	2.36 grains per gallon.	2.26 grains per gallon.

Table No. II gives the results of the mineral analysis of Scout Moor waters, with the date and place of collection of the samples. All the quantities are expressed

in parts per 100,000.

Table II.

Date of Collection.	15/10/28.	18/6/29.	3/9/29.	3/9/29.	3/9/30.
Place of Collection.	Hydrant in Edenfield.	Overflow from regulating well at Reservoir.	Regulating well where water enters main outlet.	From main intake.	Main in Haslingden.
pH value	4.0	4.3	4.3	4.4	4.0
Suspended matter.	trace	nil	heavy	nil	nil
Total dissolved solids.	6.0	6.7	10.0	8.9	7.6
Alkalinity - as Calcium Carbonate	nil	nil	nil	nil	nil
Acidity - as H_2SO_4	0.36	0.06	0.29	0.21	0.40
Chlorine	0.83	1.27	1.21	1.20	0.93
Nitric Anhydride	0.10	0.19	0.14	0.13	0.14
Sulphuric Anhydride	2.13	2.26	2.66	1.96	2.11
Silica	0.31	0.36	0.49	0.32	0.20
Oxide of Iron	0.20	0.44	0.44	0.32	0.04
Oxide of Manganese	nil	nil	-	-	0.51
Lime	0.56	0.70	0.80	0.57	0.43
Magnesia	0.63	0.77	0.79	0.76	0.81
Probable combinations.					
Free H_2SO_4	0.36	0.06	0.29	0.21	0.40
Calcium carbonate	nil	nil	nil	nil	nil
Calcium sulphate	1.36	1.70	1.94	1.39	1.04
Magnesium carbonate	nil	nil	nil	nil	nil
Magnesium sulphate	1.87	1.82	1.93	1.46	1.76
Magnesium nitrate	nil	0.26	0.19	0.18	0.20
Magnesium chloride	nil	0.21	0.21	0.52	0.40
Sodium carbonate	nil	nil	nil	nil	nil

Table II (Contd.)

Date of Collection.	15/10/28.	18/6/29.	3/9/29.	3/9/29.	3/9/30.
Place of Collection.	Hydrant in Eden-field.	Overflow from regulating well at Reservoir.	Regulat-ing well where water enters main outlet.	From main intake	Main in Hasling-den
Sodium sulphate	0.16	nil	nil	nil	nil
Sodium nitrate	0.13	nil	nil	nil	nil
Sodium Chloride	1.37	1.83	1.73	1.34	1.04
Silica	0.51	0.36	0.49	0.32	0.20
Oxide of Iron		0.44	nil	nil	0.04
Oxide of Manganese	nil	nil	0.44	0.32	0.51
Organic matter etc.	0.24	0.02	2.78	3.16	1.97
Hardness (degrees)					
Temporary	nil	nil	nil	nil	nil
Permanent	2.56	2.04	2.36	2.01	2.26
Total	2.56	2.04	2.36	2.01	2.26

as grains per gallon.

In the plumbo-solvency tests, strips of pure lead foil were immersed in 50 cc. of the water, which just covered the metal, and left for 50 hours at room temperature. The strips were then removed and any loose deposit brushed into the water with a camel hair brush. Table III shows the results of three such tests.

Table III.

Date of Collection.	Place of Collection.	Amount of lead dissolved. (in parts per 100,000).
27th March 1929.	Hydrant in Edenfield	1.62
22nd June 1929.	Overflow from the regulating well.	2.80
3rd Septr. 1930.	Main in Haslingden	1.50.

From these analyses, it will be seen that the higher parts of Haslingden are being supplied with a very soft moorland water. This water has an acid reaction, and has been shown to be capable of dissolving lead. That the action of a water on lead is dependent on the degree of acidity of the water is recognised by all authorities. Thresh (3) says that where an acid water is conveyed through lead service pipes, the consumer runs the risk of lead poisoning, and that steps should be taken to completely neutralise the water. The degree of attack on lead increases as the pH value of the water decreases, so that Scout Moor water, with a constant pH value in the neighbourhood of 4, must be expected to have an action on lead. That lead is conveyed to the consumer will be seen when the analysis of the tap water is discussed.

According to Thresh (4) acid moorland waters are

very common in Lancashire. Moorland gathering grounds are usually rich in peat and when water has been lying in contact with peat it becomes acid, and the longer it remains in contact, the more acid will it become. It follows that there will be a marked seasonal variation in the acidity of the water in the reservoir. In dry weather, the water will be less acid and may perhaps even be neutral in reaction. This is because the water then lying in contact with peat will not be washed into the collecting streams, which will derive their water principally from moorland springs, neutral in reaction, Marsden (5). But in wet weather, the acid water in the peat will be washed out, and if in any quantity will be sufficient to make the water in the reservoir acid. Examination of the water from three intakes to Scout Moor reservoir showed the pH value to be 7.4, 6.5 and 4.5 respectively, the last figure being from the main intake, which can thus be considered the source of the acidity.

From a consideration of the case histories to be presented later, one finds that most complaints arise during the summer months. I do not believe that this is simply coincidence, but that it is due to the variation in the acidity of the water during summer and winter. In winter, the continual rains are constantly washing the moorland waters into the collecting streams, so that they are not left long in contact with peat. In summer, the water may lie for weeks in the peat and so become markedly acid. But in recent years the summers have been noted for their occasional heavy rains, and these are washing out this acid water into the streams, with the result that the consumers are receiving a water with a lower pH value in summer than they are in winter. And, as we have already seen, the lower

the pH value of the water the greater is its plumbo-solvency action. Further, as these waters from Scout Moor receive no treatment whatever, the effect of the acidity will be passed direct to the consumer.

Evidence of lead in the tap water.

During the past five or six years, occasional cases of undoubted lead poisoning have appeared in the town, and it has been suspected that these cases arose from contamination of the drinking water. In one case new service pipes were installed because examination of the tap water showed that it contained one fifth of a grain of lead per gallon. From information supplied by the Medical Officer of Health, this appears to be the only occasion on which tap water has been examined for the presence of lead. The present investigation is the first attempt in Haslingden to ascertain to what extent lead poisoning is actually present in the town. Needless to say, this inquiry is limited to my own patients. As the cases are occurring in the poorer quarter of the town, among panel patients almost exclusively, the cost of all examinations made has to be borne personally. Application for facilities for the examination of tap water and of urine for the presence of lead was made to the Lancashire Insurance Pathologist, who regretted that he could not do them under the National Health Insurance Scheme. An application to the County Medical Officer of Health was referred to the town Medical Officer of Health, who promised to give every help he could in the investigation, but who, after a period of three months, has yet been unable to obtain any results. Under the circumstances, it has only been possible to examine the tap water and the urine quantitatively

in certain selected cases.

On learning that very few people are in the habit of drawing off water in the morning before filling kettles, etc., it was decided to take samples of tap water from a series of cases, this water being the first lot drawn off in the morning, i.e., the water that had been lying in the service pipe overnight. Samples were collected on two successive mornings, and submitted to Dr. Renshaw, Director of the Laboratory of Applied Pathology and Preventive Medicine, Manchester, for analysis for the presence of lead. Dr. Renshaw reported that he found lead present to such an extent that the figures would require checking by another method before being reported. He therefore submitted the samples to another analyst, requesting that the examinations be carried out by another method. The two results gave closely similar figures, as will be seen from Tables IV and V.

Table IV. - First Sample.

Case No.	Lead in parts per 100,000.	
	1st. Analysis.	2nd. Analysis.
6.	0.92	0.8
7.	0.92	1.0
9.	0.24	0.16
18.	1.12	0.8
20.	1.08	1.04
23.	0.96	0.88
24.	0.60	0.4

Table V. - Second Sample.

Case No.	Lead in parts per 100,000.	
	1st. Analysis.	2nd. Analysis.
6.	1.04	1.0
7.	0.92	1.12
9.	0.30	0.40
18.	1.16	0.8
20.	0.64	0.72
23.	0.96	1.0
24.	1.0	1.0

The first analysis was carried out by S.D.Huth, B.Sc., Chemist to the Laboratory of Applied Pathology and Preventive Medicine, Manchester, and the second analysis by G.Malcolm Dyson, Ph.D., A.I.C., Consulting Biochemist.

Since these large amounts of lead were present in the first water drawn off in the morning, it became necessary to know if lead was present in the water drawn after the service pipe had been emptied. Two samples were therefore collected from another series of cases, the first, sample (A), containing the water which had been standing in the service pipe overnight, and the second, sample (B), being collected after the water had been running continuously for five minutes. These samples were also submitted to Dr. Renshaw for analysis, and the results are shown in Table VI.

Table VI.

Case No.	Sample.	Lead in parts per 100,000.
13	A	0.8
13	B	0.2
17	A	0.52
17	B	0.1
31	A	0.8
31	B	0.1
36	A	0.88
36	B	0.1

This table is a very important one, since it was suggested by the Water Board that if consumers would run off perhaps two quarts of water in the morning before taking any for cooking or drinking purposes, there would be no further trouble with lead poisoning. Table VI proves beyond doubt that such a supposition is entirely wrong. The second samples, collected after the taps had been running continuously for five minutes, still contain lead in poisonous quantities.

That the quantities of lead found in these tap waters are poisonous is indisputable. The quantity obtained early in the morning is approximately half a grain per gallon, while that obtained after running the water for five minutes is approximately one thirteenth grain per gallon. While there is no agreement as to what amount of lead in drinking water is sufficient to cause symptoms of plumbism, all authorities agree that the above quantities are sufficient to condemn the water. Glaister (7) says, " The presence of a minute quantity of lead, even to the amounts of one tenth to one twentieth grain per gallon, is a serious matter." Gwyn (8) states that Teleky and Brouardel consider that if one milligramme is taken daily for several months, it will

cause plumbism, and that a daily dose of ten milligrammes will lead to serious intoxication. Greenburg (6) and Thresh and Beale (3) both give quotations from various authorities, but the figures vary considerably, partly owing to the fact that individuals vary in susceptibility, and partly to the difficulty in calculating how much lead is actually being consumed in any one case. Thresh (3) sums the matter up very well. He says," Probably a water containing even as a maximum one part of lead in a million would be quite safe, but at present there is no available evidence that such is the case, and where soft waters are being dealt with that take up lead from supply pipes, it would not be wise to pass a water containing one part per million unless it was perfectly certain that it was being so treated that this amount was never exceeded." That the ingestion of minute quantities of lead over a long period is more dangerous than one or two large doses taken in rapid succession, is believed by Oliver (2).

Unless a large number of examinations of tap water are being carried out, it is impossible to estimate with any degree of accuracy how much lead these cases are receiving daily. The amount of lead present is bound to vary considerably from time to time, and so render single examinations of use only in determining the presence or absence of the metal.

Cases.

In this section, the clinical details of the cases of plumbism will be related, together with the results of blood examinations and urinary findings. Where possible, the medical history has been taken from the patient's medical record card.

Case I. Mrs. A.S. aet.28. Cardroom hand.

Previous to going to her present address on the occasion of her marriage in 1922, this patient had had no illness of any kind. She has had three children, one abortion and no miscarriages. She now complains of being generally out of sorts, and of being troubled with constipation. Her appetite is good except in the mornings, when she states she has "a nasty bitter taste in her mouth."

Her previous history shows that in Septr. 1927 she suffered from very severe pains in the head. The pains were in the frontal region, and were severe enough to keep her in bed for over a week. She had a gastro-intestinal upset in 1928. The condition was diagnosed as "gastric influenza" by another doctor, and lasted throughout the months of May, June and July. In May, 1929, she had an abortion at the end of the second month.

On examination, nothing abnormal was noted in any of her systems. The patient was extremely pale, her breath was rather foul, and a blue line was noted on the lower gum. The fundi were normal. Blood pressure - 120/74.

Blood examination -

Hb.	40%
Red cells	3,312,000
Colour index	0.6
White cells	9,500
Polymorphs	67%
Lymphocytes ...	29%
Basophiles	1%
Monocytes	3%

Blood films showed the presence of 800 stippled cells per million red cells. Polychromasia, anisocytosis and poikilocytosis were present to a very slight extent only. No nucleated red cells were seen.

Urine examination -

Reaction	acid
Sp. Gr.	1016
Albumin	nil
Sugar	nil
Pus	nil
Blood	nil
Lead	present.

Tap water examination -

Lead was found to be present.

Case II. P.C. aet. 71. Labourer.

This patient resides a few doors from case No. I and had his blood film examined on the last occasion on which he came to the consulting room. 500 stippled cells were found per million red cells. On referring to his medical history, one finds that every year since 1921, this man has been seen at the consulting room, his complaint being either lumbago or dyspepsia. In 1925, during the months of July, August and Septr., he attended regularly complaining of vague pains in the abdomen, accompanied by constipation.

Case III. T.S. aet. 29. Warehouseman.

This patient has been suffering during the past few years from constipation. He was seen in June 1930 with a typical attack of lead colic. The attack had been preceded by three days obstinate constipation. When seen in the attack his blood pressure was 130/84, pulse rate 76 and his temperature 99. He was having recurring attacks of "tearing" pain in the abdomen, the situation of the pain being "all round the navel." Examination showed some tenseness of the abdominal muscles, but the patient stated that pressure was more comforting than otherwise. Teeth very decayed, but no blue line present.

Blood examination -

Hb.	44%
Red cells	3.807,500
Colour index	0.6
White cells	13,000
Polymorphs	57.5%
Lymphocytes	31.5%
Eosinophiles	2%
Basophiles	1%
Monocytes	8%

Examination of the blood film showed that stippled cells were present to the extent of 16,000 cells per million red cells. Polychromasia, anisocytosis and poikilocytosis were present to a slight degree only, while no nucleated red cells were seen.

Urine examination -

Reaction	acid
Sp. Gr.	1012
Albumin	nil
Sugar	nil
Pus	nil
Blood	nil
Lead	present.

Tap water examination -

Lead was found to be present.

Case VI. J.J.B. aet. 37. Twister.

During July, August, Septr. and Octr. of 1925, this patient suffered from obstinate constipation, the condition being diagnosed "intestinal stasis" by another doctor. In July, 1927, he had an attack of colic, accompanied by obstinate constipation of five days' duration and by vomiting. During the colic the patient was bathed in cold perspiration, and was extremely restless. In Octr. 1927, he began to complain of pains in the arms andlegs, and within a fortnight he had complete bilateral wrist-drop. Examination of blood films showed large numbers of stippled cells. Treatment was carried out at the local Massage

Centre, and by Septr.1928 the patient was able to return to his work. In Octr. 1929, he again returned with bilateral wrist-drop. It appeared that in spite of all warnings, he had dropped into the habit of using the tap water again. Blood films again showed many stippled cells, and in spite of the improvement in the extensor muscles since then, every blood film examined up-to-date shows many stippled red cells.

Blood examination June, 1930 -

Hb.	40%
Red cells	3,500,000
Colour index	0.6
White cells	8,900
Polymorphs	70%
Lymphocytes	24%
Eosinophiles	2%
Basophiles	nil
Monocytes	4%.

The blood film shows very little polychromasia, anisocytosis and poikilocytosis, and no nucleated red cells were seen. 70,000 stippled cells were present per million red cells.

Urine examination -

Reaction	Acid
Sp. Gr.	1020
Albumin	nil
Sugar	nil
Pus	nil
Blood	nil
Lead	present.

Tap water examination -

Lead has been found present to the extent of 0.92 and 1.04 parts per 100,000 respectively.

Blood pressure 140/90. The fundi are hyperaemic. Artificial dentures are worn, the teeth having been extracted after the first attack of colic.

Case VII. J.W.G. aet. 61. Weaver.

This patient was first suspected to be suffering from lead poisoning in March, 1930, when he was seen with a slight impairment of extension of the middle and ring

fingers of the right hand. A blood film showed the presence of punctate basophilia. Within a fortnight he had developed complete bilateral wrist-drop. On enquiring into his past history, one finds that in Septr. and Octr. 1926, he suffered from dyspepsia and constipation. In Octr. 1928, he again suffered from dyspepsia. In 1929, from June to Octr. he again had dyspepsia, and the true nature of the condition not being recognised, the gastro-intestinal tract was radiographed, with negative results. Blood pressure 170/90. Fundi normal. Teeth were extracted in Octr. 1929.

Blood examination, March, 1930.

Hb.	55%
Red cells	2,687,000
Colour index	1.0
White cells	8.500
Polymorphs	63%
Lymphocytes	30%
Eosinophiles	2.5%
Monocytes	4.5%

Punctate basophilia was noted in 14,000 cells per million, while polychromasia, anisocytosis and poikilocytosis were quite marked.

Urine examination.

Reaction	Acid
Sp. Gr.	1020
Albumin	nil
Sugar	nil
Pus	nil
Blood	nil
Lead	present.

Tap water examination.

In two examinations lead was found to the extent of 0.92 and 1.12 parts per 100,000 respectively.

Case IX. W.B. aet. 38. Labourer.

This patient was first seen in Novr. 1929 with an attack of acute abdominal colic, with constipation and vomiting. The condition was very severe. The patient was

quite ashen looking, and presented all the appearances of an abdominal catastrophe. The abdominal wall was rigid, and palpation appeared to be resented. As the patient resided in the suspected area of the town, a blood film was examined, and the presence of marked punctate basophilia indicated the treatment. In June, 1930, he had a similar attack, also accompanied by vomiting and constipation. Blood pressure 140/84. Fundi normal. Teeth are bad but no blue line on the gum.

Blood examination.

Hb.	58%
Red cells	4,375,000
Colour index	0.7
White cells	12,000
Polymorphs	69%
Lymphocytes	26%
Eosinophiles	2%
Monocytes	3%

The blood film showed stippled cells to the extent of 600 per million red cells. No nucleated cells were seen.

Urine examination.

Reaction	Acid
Sp.Gr.	1010
Albumin	nil, but faint haze has been found on occasion.
Sugar	nil
Pus	nil
Blood	nil
Lead	present.

Tap water examination.

Two examinations of the tap water were carried out, and showed lead to be present to the extent of 0.24 and 0.40 parts per 100,000.

Case X. Mrs. W.B. aet. 35. Weaver.

This patient is the wife of case No. IX, and for this reason her blood was examined for the presence of punctate basophilia. Her only complaint is that during the past two years she has been troubled with severe headaches.

Blood examination.

Hb.	50%
Red cells	3,000,000
Colour index	0.8
White cells	11,500
Polymorphs	66%
Lymphocytes	32%
Monocytes	2%

Urine examination.

Reaction	Acid
Sp. Gr.	1022
Albumin	nil
Sugar	nil
Pus	nil
Blood	nil
Lead	present.

Tap water examination.

Lead present as in case No. IX.

Case No. XIII. H.K. aet. 42. Railway porter.

This patient has been a chronic invalid since 1921, suffering continuously from a dyspepsia for which no organic cause could ever be found in spite of repeated radiographic examinations of the alimentary tract. Three years ago he developed asthma. In Septr. 1927, he had to be admitted to a mental institution suffering from hallucinations. In June 1930 a blood film was examined and stippling was found to be present in a large number of the red cells. The urine shows the presence of lead, and lead has been found in the tap water to the extent of 0.2 parts per 100,000 after the water had been allowed to run to waste for five minutes.

Case No. XV. Mrs.J.J.B. aet.35. Weaver.

This patient is the wife of Case No.VI. A blood film shows the presence of punctate basophilia. The patient presents the deadly ashen hue common among these cases, but otherwise does not complain of anything.

Case No. XVII. Miss E.J. aet.52. Weaver.

This patient has been suffering from neuritis, dyspepsia and constipation at very frequent intervals since April 1927. Radiograms revealed no abnormality of the digestive tract, and repeated examinations failed to find evidence of organic disease. On two occasions the patient has been slightly jaundiced, and in June 1930 she had mild abdominal colic. A blood film was examined and stippling found to be present.

Blood examination.

Hb.	60%
Red cells	2,500,000
Colour index	1.2
White cells	6,250
Polymorphs	68%
Lymphocytes	23%
Eosinophiles	4%
Basophiles	1%
Monocytes	4%

Examination of the blood film showed that stippled cells were present to the extent of 17.000 per million red cells.

Urine examination.

Reaction	Acid
Sp.Gr.	1020
Albumin	nil, but occasionally a faint haze is seen.
Sugar	nil
Pus	nil
Blood	nil
Lead	present

Tap water examination.

After being run to waste for five minutes, the tap water contained 0.1 parts of lead per 100,000. This patient stated definitely that she never ran off water before filling the kettle in the morning, and examination of this water showed that it contained 0.52 parts of lead per 100,000.

Case No. XVIII. J.T.McG. aet.55. Stripper and Grinder.

This patient has lived at the one address for the past 36 years. The water supply was put into the house over

thirty years ago, and the patient states that there has been no alteration to the service pipes since then. During the past fifteen years the patient has suffered from periodical attacks of backache, constipation, and severe abdominal pain. The abdominal pains were called "colic" by his doctor, and were always bad enough to keep him in bed for ten to fourteen days at a time. Early in 1925 he was sent into hospital for observation, having been suffering from vague abdominal pains for over three months. A laparotomy was done, nothing abnormal was found, and his appendix was excised. Within a month of returning home, his condition was as bad as ever. The vague abdominal pain was still complained of, but as time went on, the symptoms became more definite. They began to have a time relation to the taking of food, coming on definitely about two hours after food, and being relieved by taking more food. Radiograms showed no evidence of duodenal ulceration. At his own request, he was returned to hospital for observation, and this time a gastroenterostomy was performed. The patient came under my care some six months after the gastroenterostomy. He looked ill, being very pale and obviously having lost a great deal of weight. His complaint was now referable to the gastroenterostomy, the patient stating that he could take no solid food of any kind, and that twice a week he was very sick, the vomitus being a large quantity of apparently digested food. Radiograms taken about twelve months ago showed narrowing of the stoma. Further operative treatment was not advised, the patient went from bad to worse, and three months ago he was confined to bed. At this time blood films were examined and showed the presence of large numbers of stippled cells. An examination of the

tap water showed on two occasions the presence of lead to the extent of 1.12 and 1.16 parts per 100,000 respectively. Later the patient had to be removed to hospital for adequate nursing, and I am informed that he died there about one month later.

Case NO. XIX. R. McG. aet. 26. Weaver.

This case is a son of case No. XVIII. His blood shows the presence of stippled cells. Except for influenza in 1925 and 1927, there is no record of any illnesses. Lead is present in the tap water.

Case No. XX. M.H. aet. 64. Charwoman.

This patient suffers from chronic bronchitis and neuritis. The neuritis affects principally the arms, and when present is severe and disabling, the patient stating that she has difficulty in holding things. Examination of blood films shows the presence of stippled cells, while in two samples of tap water, lead was found to the extent of 108 and 0.64 parts per 100,000 respectively.

Case No. XXIII. J.J. aet. 64. Quarryman.

This patient had his first attack of intestinal colic in 1925. He had another attack in 1929, suffering from severe colic, vomiting and constipation. After this attack the constipation became chronic, he was continually having pain in the abdomen, and he lost considerable weight. Repeated examinations failed to elicit signs of organic disease, and radiographic examination of the whole alimentary tract was entirely negative. Early this year his blood was examined, and the cause of all the trouble shown by the presence of stippled cells. Examination of two samples of tap water

showed that each contained 0.96 parts of lead per 100,000. Since being informed that the tap water was the cause of the trouble, this patient has used only spring water, and his general condition has improved considerably, each week showing an increase of weight, and his abdominal discomfort disappearing completely.

Case No. XXIV. C.W.P. aet. 51. Plumber.

In 1926, this patient was found to be suffering from syphilis, his Wasserman being positive I in 15. He has been suffering for some considerable time from headaches and dizziness, and at times is very forgetful. Being resident in the suspected area, his blood was examined and stippling found to be present. Two samples of the tap water were examined, and lead was found to the extent of 0.60 and 1.0 parts per 100.000 respectively.

Case No. XXV. Mrs. M.T. aet. 47. Weaver.

This patient has been suffering from chronic constipation since 1922, and has been considered very neurasthenic on account of her never-ending complaints, especially of severe headaches confined to the top of her head, for which no cause could be found. In January, 1930, this headache became intolerable, and proved resistant to all treatment. One morning she suddenly left her work, and without giving any reason, walked out of the mill. As this was a most unusual proceeding, it occasioned some comment, and when she did not return it was decided to send someone to find her. Two hours later the patient was found walking into Blackburn, a distance of 8 miles away. When found, she was very confused, had no idea of where she was or of how

she had got there, and was only concerned about the severe pain in her head. Blood films were examined and stippled cells found in large numbers. The tap water in this case was not examined, but a 24 hour specimen of urine was examined quantitatively for lead. This was found to be present to the extent of 0.6 milligrammes per litre. The urine did not contain albumin. A few epithelial cells were present, but no casts.

Case No. XXVI. J.W.W. aet.24. Reedmaker.

In 1929, and again in June, 1930, this patient had attacks of lumbago. Blood films were examined, and stippled cells found present in large numbers. The tap water was not analysed, but a 24 hour specimen of urine was examined quantitatively for the presence of lead. This specimen did not contain lead, and was negative for albumin, cells and casts.

Case No. XXVII. Miss S.J.P. aet.26. Weaver.

This patient is the daughter of Case No. XXIV. Except for influenza in 1924, 1926 and 1929, the patient has no medical history. Blood pressure 120/74. A blue line is present on the lower gum.

Blood examination.

Hb.	65%
Red cells	4,000,000
Colour index	0.8
White cells	10,000

Examination of a blood film shows the presence of a large number of stippled cells. Lead is present in the tap water as in Case No. XXIV

Case No. XXVIII. J.McG. aet.3I Spinner.

Case No. XXIX. D.McG. aet.30 Cardroom hand.

Case No. XXX. T.McG. aet.19 Weaver.

These three brothers had films examined because they were resident in the suspected area. All showed the presence of punctate basophilia. Lead was present in the tap water as in Case No. XVIII.

Case No. XXXI. Mrs.H.A. aet.28. Weaver.

This patient has been married for eight years, and has one child aged seven. (Case No. LVI) In March 1929 she had an abortion, and another in July 1930. In each instance the abortion took place at the end of the second month. After the second abortion, a blood film was examined, and showed the presence of a large number of stippled cells. Blood pressure 122/80. The fundi are normal. A blue line is present on the gum under the six lower front teeth, an artificial denture being worn on the top. Examination of the tap water showed that it contained 0.8 parts of lead per 100,000 in the morning before any had been run to waste, and 0.1 parts per 100,000 after running for five minutes. In this case the first water in the pipe was habitually used for cooking for breakfast. A quantitative analysis of the urine was carried out by Dr. Renshaw, who reported that lead was found to the extent of 0.2 milligrammes per litre. The urine contained a faint trace of albumin, some epithelial cells and a few pus cells. An odd red blood cell was also seen. There were no casts.

Case No. XXXVI. W.W. aet.55. Weaver.

In 1927, this patient was treated by another doctor from August to December for dyspepsia. In January, 1930, he

suffered from muscular pains. In June he complained of "severe nagging pains" in the abdomen, generally about the umbilicus. He also had anorexia and constipation. A blood film showed the presence of punctate basophilia. On 1st. September he developed a definite paralysis of the middle and ring fingers of the right hand. Three weeks later, it was noted that the paralysis had not made further progress. Lead is present in the urine, and has been found in the tap water in the early morning to the extent of 0.88 parts per 100,000. Blood pressure 190/110. Fundi normal. No blue line was to be seen.

Case No. XXXVIII. D.B. aet.23. Cardroom hand.

A blood film was examined because the patient resided in the suspected area, and stippled cells were found present. A blue line is present under the two lower central incisors. Fundi normal. Blood pressure 118/52.

Case No. XL. Miss C.B. aet.27. Ringspinner.

A sister of Case No. XXXVIII, and examined for the same reason. Stippled cells were found present. There is no previous medical history.

Case No. XLI. Mrs.A.W. aet.26. Housewife.

This patient has always been troubled with dysmenorrhoea, but the condition has been very much worse since she came to reside in Haslingden eighteen months ago. She has apparently healthy and clean teeth, and states that she takes great care of them, but a distinct blue line is present under the two lower central incisors.

Blood examination.

Hb.	65%
Red cells	4,200,000
Colour index	0.8
White cells	7,500

Examination of a blood film shows the presence of punctate

basophilia.

Case No. XLII. Mrs.C.T. aet.60. Weaver.

During the past few years this patient has been very troubled with neuritis and severe headaches. Since she is resident in the suspected area, a blood film was examined and stippling found present.

Case No. XLIII. G.R.D. aet.48. Bobbin carrier.

This patient was first seen in July, 1930, when he complained of constipation and abdominal colic. His teeth are bad, his breath foul, and a blue line is present on the lower gum. Physical examination of the abdomen was negative.

Blood examination.

Hb.	63%
Red cells	3,350,000
Colour index	0.9
White cells	11,250

Examination of a blood film showed the presence of many stippled cells.

Case No. XLIV. Mrs.A.B. aet.45. Weaver.

Since 1927, this patient has had many attacks of neuritis in her arms. In November, 1929, pulmonary tuberculosis was diagnosed, and the patient admitted to a sanatorium on 9th. December, 1929. This patient is resident in the suspected area, and during her absence her son (Case No. XIV) was found to have punctate basophilia. Immediately on her return from the sanatorium on 20th. July, this patient's blood was examined and stippled cells found present. The patient has upper and lower artificial dentures.

Case No. XIV. T.B. aet.21. Weaver.

Case No. XLVI. Miss S.B. aet.24. weaver.

These two cases are respectively son and daughter of case No. XLV. and examinations of blood films from both show the presence of stippled cells. Neither shows the presence of a blue line on the gums.

Case No. XLVIII. G.W. aet.74. Weaver.

This patient is very troubled with constipation. Examination of a blood film shows the presence of stippled cells. Upper and lower artificial dentures are worn.

Case No. XLIX. H.K. aet.26. Labourer.

During the past two years this patient has been troubled periodically with muscular pains. After an infective condition of the fingers, he developed bilateral wrist drop. There is no blue line, but the patient is extremely pale. Blood films show the presence of stippled cells in large numbers.

Case No. L. Miss E.W. aet.20. Weaver.

This patient has been troubled with obstinate constipation since November, 1928. Examinations of the abdomen have revealed nothing abnormal, while radiographic examinations of the whole alimentary tract have been negative. Every endeavour has been made to correct the constipation, but has met with no success. It was not until early this year that lead poisoning was suspected, and examination of blood films showed the presence of punctate basophilia.

Blood examination.

Hb.	60%
Red cells	4,000,000
Colour index	0.7
White cells	6,250

There is no blue line on the gums.

Case No. LIII. H.A. aet.26. Cardroom hand.

Case No. LVI. J.A. aet.7.

These cases are respectively husband and son of Case No. XXXI. Because of the presence of lead in the tap water blood films were examined from both cases, and stippled cells were found in each.

Case No. LIV. Miss S. McL. aet. 34. Weaver.

When this patient came to ask advice regarding dental treatment, it was noted that a blue line was present on the lower gum. Examination of blood films showed that stippled cells were present to the extent of 18.000 per million red cells.

Blood examination.

Hb.	50%
Red cells	3,500,000
Colour index	0.7
White cells	10,000
Polymorphs	53%
Lymphocytes	36%
Eosinophiles	4%
Basophiles	1%
Monocytes	6%

Case No. LVII. Mrs.L.C. aet.40. Weaver.

This patient complains of intense headaches, particularly over the vertex. She states that she is never entirely free from headaches, and that during the past two or three years she has not enjoyed good health. In November 1928, she had an abortion at the end of the second month. The Wassermann reaction is negative.

Blood examination.

Hb.	58%
Red cells	3,750,000
Colour index	0.8
White cells	9,000
Polymorphs	54%
Lymphocytes	36%
Eosinophiles	2%
Basophiles	1%
Monocytes	7%

Examination of the blood film showed that stippled cells were present to the extent of 6,000 per million red cells. An examination of the tap water was not carried out, but a 24 hour specimen of the urine was submitted for examination, and was found to contain lead to the extent of 0.4 milligrammes per litre. There was no albumen, but some epithelial cells and two or three pus cells were present. There were no casts.

Case No. LVIII. C.G. aet. 52. Cardroom hand.

Because of failing eyesight, this patient consulted an ophthalmic surgeon, who referred him to me for treatment for suspected tobacco amblyopia. As the patient never touches spirits, is a very moderate beer drinker, and only smokes 4 oz. of tobacco per week, and particularly because he resides in the suspected are, it was decided to investigate the case for possible lead poisoning. There is slight impairment of vision, V.A. being 6/12 in both eyes. The retinal veins are congested. There is neither albuminuria nor glycosuria. The teeth are bad and few in number, but there is no blue line. Blood pressure 170/85.

Blood examination.

Hb.	65%
Red cells	3,250,000
Colour index	1.0
White cells	20,000
Polymorphs	52%
Lymphocytes	38%
Eosinophiles	5%
Basophiles	1%
Monocytes	4%

Examination of blood films showed that stippled cells were present to the extent of 7,000 per million red cells. The tap water was not examined, but a 24 hour specimen of urine was submitted for analysis. This specimen did not contain lead, albumen, cells or casts.

When one comes to study the history of these cases of chronic plumbism, one finds that certain symptoms recur again and again. These common symptoms will be discussed in the following section.

Anaemia.

All the patients in this series of cases showed marked pallor of the tissues. With perhaps two exceptions (Cases No. XXIII and XXV) none of the patients presented even the slightest tinge of colour. The lips were of a faint bluish hue. In every blood count, there was a reduction in the number of erythrocytes, the lowest count obtained being 2,500,000 (Case No. XVII). It was noted in all the blood films that irrespective of the number of red cells present neither anisocytosis nor poikilocytosis was very marked. In cases of secondary anaemia due to excessive loss of blood, one would find these two conditions much more marked than in chronic plumbism. While polychromasia was present in most films, it was never found in any marked degree. But it has to be remembered that the change of colour between normal red cells and polychromatic cells may be so slight as to render it difficult to say whether the condition is present or not. Like the reduction in the number of erythrocytes, the reduction in the percentage of haemoglobin was very noticeable. This showed a reduction in all cases, and was markedly reduced in some. It gave the cells a characteristic appearance, the cells appearing like rings, with the periphery of the cell showing clearly with the acid stain, and the centre of the cell almost colourless. This appearance could be demonstrated in almost every film. But the most noticeable change in the erythrocytes was the presence of punctate basophilia. This was found in every case in the series, and will be discussed later.

Nothing significant was noted in the leucocytic count nor in the differential count. All the counts were normal, the highest figures obtained being within the limits of physiological increase. In no case was there a leucopaenia. The percentages of the various white cells did not throw any light on the nature of the pathological process at work. Any tendency to an increase was shown by the large mononuclear cells, but the number of cases investigated is too small to place any significance on this.

Taking the complete blood findings into account, one has difficulty in co-relating the blood changes with the extraordinary pallor shown by these cases. That lead in some way is responsible for the pallor is believed by many authorities. The exact cause of the pallor is not known, but Koelsch (9) believes that it is partly due to the action of lead on the skin capillaries.

Gastro-intestinal symptoms.

In the majority of cases, dyspepsia of some kind had been complained of during the period covered by this investigation. While all types of dyspepsia are met with, most cases give a history almost identical to that of duodenal ulcer. These patients complained of pain coming on about two hours after taking food, stated that the pain lasted for some time, and was relieved by taking more food. In none of the cases was the pain troublesome in the middle of the night. Examination usually revealed a clean tongue. In most cases nothing was to be found in the abdomen, but in some there was definite tenderness in the epigastrium. A few of the cases so simulated organic disease that it was thought necessary to have radiographic examinations of the alimentary tract carried out. In all the results were negative. All

the cases in this group proved to be very resistant to treatment.

Some patients did not describe the symptoms of dyspepsia, but complained more of indefinite pains in the abdomen. These pains could not be localised to any one part of the abdomen, and did not have any relationship to the taking of food. Physical examination of the abdomen was quite negative.

Most patients were troubled with constipation. It was not uncommon to hear that the bowels only acted every third or fourth day, the favourite household and proprietary remedies proving to be quite useless. None of the cases exhibited the intermittent diarrhoea stated by Legg and Goadby (10) to occur in 15% of cases.

By far the most striking gastro-intestinal symptom was the occurrence of colic. Eight patients in this series had colic, most of them having more than one attack. The attack was always preceded by three to five days obstinate constipation. When seen in the attack, these patients looked extremely ill, and the diagnosis of the condition gave rise to a great deal of anxiety in some. The complaint is of intense, agonising pain in the abdomen, accompanied by vomiting and constipation. The patients are deadly pale, and are usually found lying flat in bed with their knees drawn up. They cannot localise the pain, but say that it is all over the lower abdomen. The abdominal muscles are so rigid that palpation is almost impossible. Only one case ever admitted that pressure on the abdomen relieved the pain. During the paroxysm the patient is restless, but not to the extent seen in renal colic. The mere fact of the patient being restless does not help the diagnosis. I have seen cases of perforated gastric ulcer far more restless than these cases of lead colic

In the absence of a knowledge that lead intoxication is prevalent, the diagnosis between some abdominal emergency and lead colic can be most difficult. The signs and symptoms may not be typical of an acute abdominal catastrophe, but they simulate it so much that one is left in doubt. Especially is this so when one is in the habit of seeing perforations of some of the viscera within half an hour of their occurrence, when the signs are by no means definite.

Neuritis.

In a number of the cases complaints were made of neuritis. This most commonly affected the arms, but in some cases affected the lower limbs as well, and in others was confined to the intercostal nerves. Acute pain would be complained of in the upper arm of forearm, and occasionally in the whole arm. The pain was often accompanied by tingling and numbness in the fingers. The condition always appeared to be worse during the night. In no case was any sensory disorder noted.

Paralysis.

In four of the cases some degree of paralysis developed. In one case there had been previous attacks of lead colic. Pains and weakness in the arms and legs preceded the onset of the paralysis. In one case, complete bilateral wrist-drop developed in the course of six to seven days. In none of the other cases has the paralysis been so complete. In two, weakness of the extensor muscles of the hand was first complained of, and in the course of fourteen to fifteen days this developed into paralysis of the middle and ring fingers of the right hand. In one of these cases the middle and ring fingers of the left hand became affected later.

Headaches.

The headache complained of in this series of cases was of a very severe character, and proved very resistant to treatment. The pains were commonly present in the vertex, although some had pain in the frontal and occipital regions. In these cases the eyes were examined for errors of refraction, heart and lungs examined for organic disease, and the urine examined for evidence of kidney disease. The headaches were generally worse in the mornings, but in some cases were so severe in the night as to cause insomnia.

Lumbago and Muscular Pains.

Where these were present the patients had many attacks. There was nothing unusual about the lumbago. The general muscular pains, which did not always accompany the lumbago, appeared to be very disabling. The condition was quite afebrile. Legge and Goadby (11) regard complaints of lumbago in lead workers seriously, and consider that such complaints may be a guide in discovering an early intoxication. The muscular pains were principally felt in the lower limbs, and were described as being "cramp-like". They tended to be worse during the night, the patient "not knowing where to put his limbs to get them comfortable."

Abortions and Menstrual Disturbances.

In this series four abortions occurred in three patients. The W.R. in each case was negative. All four abortions occurred at the end of the second month or early in the third month. In this connection, it should be mentioned that it is generally accepted that the abortion rate in Haslingden is high. My colleagues all speak of the apparently

large number of abortions that occur among their patients, but, until now, no suggestion has been made as to the cause of this. Oliver (12) says, "An increase in the number of miscarriages or of still-births in a town or district should cause medical men to suspect either lead in the drinking water or in drugs taken surreptitiously."

Other menstrual disturbances complained of include amenorrhoea, menorrhagia and dysmenorrhoea.

Encephalopathy.

In only one case was there any suggestion of lead encephalopathy. (Case No. XXV.) Here the condition did not go on to convulsions. Unfortunately the patient had been treated as a neurasthenic for some considerable time before it was discovered that she was suffering from lead poisoning.

Amblyopia.

In only one case did this occur, and some difficulty was experienced in deciding whether it was due to lead or to tobacco. As lead was absent from the urine examined, the diagnosis of the case became more difficult. But as time went on, one or two things pointed to lead as being the cause of the trouble. The blood showed the continued presence of stippled cells - up to 7,000 per million red cells. The condition of the eyes improved in spite of the continued use of tobacco, and the patient's general condition improved when he ceased to use the tap water.

The presence of Lead in the Urine.

It must again be remarked that owing to the cost of quantitative urinary analysis by a competent analyst, very

few of these examinations could be carried out. In some of the cases, where punctate basophilia was the only indication of lead poisoning, and where the tap water had not been analysed, it was thought desirable to have reliable examinations of the urine carried out. In each case a twenty - four hour specimen was obtained. The urines were submitted to Dr. Renshaw of Manchester, and the results of the analysis are shown in the following table, -

Table VII.

Case No.	Lead in milligrammes per litre.
25.	0.6
26.	nil
31.	0.2
57.	0.4
58.	nil

It is to be regretted that more of these examinations could not be carried out, especially as qualitative tests to detect the presence of lead in urine are so very unsatisfactory. Many of the qualitative tests were tried, but none of them proved very reliable.

With regard to the excretion of lead in the urine, it has to be remembered that the greatest proportion of lead ingested passes through the gastro-intestinal tract without ever being absorbed. Most of the lead absorbed from the gastro-intestinal tract is taken to the liver by way of the portal circulation, and is excreted in the bile without being taken into the general circulation. Any lead appearing in the urine is therefore an index of the presence of lead in the systemic blood, and, as we have seen, this is a minute

proportion of that ingested. But this presence of lead in the urine assumes great significance, because it indicates that lead is actually being absorbed into the system. Kehoe (13) noted that healthy men, many of whom had had no definite exposure to lead, excreted lead normally in the urine and faeces. The quantity present in the urine in these cases is infinitesimally small, and is only detected by the most exact methods of analysis. Blair Bell (14) investigated the question of lead excretion in the urine in his cancer cases where lead had been given intravenously, and he came to the conclusion that the lead found was not greater in quantity than that found in healthy adults. He states that there is , therefore, no evidence that any of the lead injected is being excreted in the urine. His average figure for four healthy persons is 0.056 milligrammes of lead per litre of urine, a figure readily distinguishable from the figure obtained where lead is being excreted in pathological amounts.

That lead can be excreted through the kidneys for some time without causing the appearance of albuminuria, is also recognised. There is a noticeable absence of albuminuria in this series of cases, even when definite evidence of plumbism is present. Blair Bell (15) has noticed that with lead nephritis the urinary excretion may be reduced by one half and contain an appreciable quantity of lead, without the appearance of albuminuria.

The Blue Line.

The presence of a blue line on the gums was noted in six of my cases. I am convinced that it would have been seen oftener had not so many of the cases taken advantage of the National Health Insurance Benefits, and had their teeth

extracted and artificial dentures fitted. The majority of the patients had artificial dentures top and bottom, and all stated that prior to having dental treatment their teeth had been very bad.

Most writers state that if the teeth are kept clean a blue line will not develop. In two of my cases (XXXI and XLI) both patients were most emphatic in stating that the teeth were cleaned daily, and from the appearance of the teeth, I have no reason to doubt their statement. Yet in both, a well marked blue line was to be seen. This line could not be rubbed off. Neither patient had been taking bismuth. In case No. XLI the blue line was only to be seen in the gum under the lower two central incisors, while in case No. XXXI, it was present below the lower six front teeth. Aub (16) describes the blue line as probably the most characteristic and common finding in lead poisoning. It appears as a dark line near the edge of the gum close to the teeth. That it is not situated on the gum is proved by the fact that it cannot be rubbed off. Some authors state that it may be seen in the mucosa of the lip or cheek opposite decaying teeth, but such staining has not been noted in any of my cases. The only other condition in which a blue line might be seen is bismuth poisoning, so that the appearance of the line becomes practically diagnostic.

All the theories put forward to explain the formation of the blue line believe that it is caused by the interaction of dissolved lead and hydrogen sulphide, resulting in the formation of black lead sulphide. The lead is believed to be carried to the gums in the blood stream, while the hydrogen sulphide is thought to result from the decomposition of food material left between the teeth, and from the decaying tissues around bad teeth. How the lead and the hydrogen

sulphide come together, and by what process lead sulphide is formed, is now known. It was at one time thought that lead was brought to the gums by being secreted in the saliva, but as no evidence of the presence of lead in the saliva has ever been satisfactorily produced, this theory cannot be upheld.

Blood pressure.

It is generally accepted that long exposure to lead and its consequent absorption in small doses leads to an increase of blood pressure. In the present series of cases, frequent blood pressure estimations have been made. In any case with a heightened blood pressure, other factors than lead poisoning have been found to account for it. In Case No. XXXI, where traces of albumin have been found occasionally in the urine, the blood pressure has never shown an increase over the normal.

Punctate basophilia.

Punctate basophilia, or stippling, is a condition in which numerous small basophilic granules are found in the protoplasm of certain red blood corpuscles. It can be demonstrated by fixing and staining a blood film with any of the Romanowsky group of stains. All the films examined in the present investigation were stained by Pappenheim's method, described by Piney (17).

Examined under an oil-immersion lens, punctate basophilia is seen as small dark blue granules scattered throughout the red cell. The size of the granules varies in different cells, some being very fine and small, and others quite coarse and large. All variations in size may be seen on one film. In all the films I have examined, the granules

have been circular in shape, but Brookfield (18) states that in the coarser form, bar-shaped forms may appear. These have also been noted by Cooke (19). In some erythrocytes, the granules are scattered uniformly throughout the cell, while in others they are confined to the periphery. The latter appearance is especially seen where there is deficient haemoglobin in the cell, the cell having the appearance of a ring. The number of granules in the cell varies considerably, from four to five up to as many as thirty.

Since punctate basophilia was first described by Ehrlich (20) in 1885, a great deal of controversy has arisen over the origin of these granules. Ehrlich's original theory was that they were derived from the cytoplasm, but in 1893, Askanzy (21) believed that he could demonstrate all transitions between polychromasia, stippling, karyorrhexis and karyolysis, and he formulated the theory that the granules arose from nuclear material. The modern view agrees with the original theory of Ehrlich, and has been supported by Grawitz (22), Schilling-Torgau (23), Pappenheim (24), Brookfield (18), Cooke (26), and Aub (27). All these workers uphold the theory on the following grounds -

(a) When nucleated red cells are present in the blood stream, their cytoplasm may contain granules while the nucleus remains quite intact.

(b) The staining reactions of nuclear material and of the granules is quite different.

(c) While the granules are transparent to ultra-violet light, nuclear material is opaque.

With this evidence it may fairly be held that the granules in punctate basophilia are derived from the cytoplasm of the cell.

Having established the origin of the granules, the question arose as to whether the reaction was due to degeneration or to regeneration. Because of the appearance

of stippled cells in the embryo, Engle (28) believed that their presence in the adult signified a return to the embryonic type of blood, and that, therefore, it was a regenerative reaction. But this view is no longer held. The absence of punctate basophilia from the bone marrow has been demonstrated by Key (29) and this, with the fact that stippling only occurs in pathological conditions, would indicate that it is a degenerative process.

To understand fully the nature of punctate basophilia, it is necessary to refer to its relation to other basophilic substances in the cytoplasm of the erythrocyte. These are seen in the conditions of polychromasia, or polychromatophilia, and reticulation.

Polychromasia is the name given to the red cells which take on a bluish colour with ordinary blood stains. The colour is diffused throughout the cell. Such cells are normally found in the bone marrow and their presence in the peripheral blood stream is taken as an indication of bone marrow activity. That is, they are young cells. Polychromasia is therefore to be regarded as a regenerative process. The condition is seen in all severe anaemias, and is constantly seen in association with stippling.

Reticulation can only be demonstrated by methods of vital staining. It appears as a deeply stained network in certain red blood cells, the actual form found depending on the stain used. It always appears in the same conditions as produce polychromasia. Brookfield (18) by counting the number of polychromatic cells and stippled cells, and the number of reticulocytes, and expressing the result as a percentage of the total red cells, found that there was a numerical agreement, the polychromatic cells plus the stippled

cells being equal to the reticulocytes. He believes that these cells are fundamentally the same, the only difference being their method of demonstration. The relationship between the three conditions is that all three are simply different stages in the same process. It is worthy of note that Cooke (26), in an attempt to explain why the different appearances occur, found that by using benzidine and hydrogen peroxide, he could produce all three conditions in any erythrocyte. With our previous knowledge of staining reactions, he infers that the three conditions are qualitatively the same, and vary only in degree.

Stippled cells are, therefore, a manifestation of a degenerative process acting on young erythrocytes. That the damage takes place in the peripheral blood stream is shown by the fact that stippled cells have never been demonstrated in the bone marrow.

The association of punctate basophilia with lead poisoning was first pointed out by Behrend (32) in 1899, and since then has received ample confirmation. Aub's work (16) has demonstrated without question the occurrence of punctate basophilia in lead poisoning, and he states that his experience is that stippling is the most reliable of the early signs of lead intoxication. Blair Bell, Williams and Cunningham, (34) in their treatment of cancer by intravenous injections of colloidal lead, examined the blood of every case before, and at varying intervals during, treatment, -- "especially for the presence of stippled red blood corpuscles". The results of their work form a most important addition to our knowledge of the effects of lead on the blood. From their observations they state that they attach a great deal of importance to the presence of punctate basophilia as a sign of lead poisoning.

so much so, that they deem it inadvisable to give further lead injections if the stippled cells are in the neighbourhood of 2% of the total number of red cells. Brookfield (18) states that stippling is a constant feature in patients receiving lead injections, and that its extent is the most valuable index of the degree and severity of the lead intoxication induced. He states that it occurs to such a degree and so frequently that it is a sign of great importance.

But the presence of stippling is not a specific sign of lead poisoning. It occurs in pernicious anaemia, in leukaemia, in the anaemias due to the cachexia of neoplasms, and in malaria. It has also been observed in cases of aniline poisoning. Sabraze (36) made the observation that it occurred in apparently healthy adults, but Blair Bell, Williams and Cunningham (34), do not agree with this, as they found it in only one single case in a large series of blood examinations before lead was administered. The occurrence of stippling in these other conditions should occasion no difficulty. Its presence there is slight compared with its intensity in lead poisoning, and, moreover, the other symptoms present will enable the condition to be diagnosed without depending on the presence of stippling. It would therefore appear that stippling is a sign of great importance in lead poisoning, and that in its presence, this intoxication should be carefully borne in mind until all possibilities of its occurrence have been ruled out.

According to Stainthorpe (37), the absence of stippled cells does not of itself negative a diagnosis of lead poisoning. Giving his observations on one hundred and twenty cases of lead poisoning from drinking water in an epidemic at Guisborough, he states that "thirty cases were carefully

examined for the presence of basophilic staining granules in the red cells, with negative results." Films from his series of cases were examined by Sir Thomas Oliver and by Sir Kenneth Goadby, also with negative results. In each of his cases the diagnosis was based on the presence of lead in the urine. Oliver (38) states, "as basophilia is not always present, even in cases of lead poisoning which are beyond question, and since, too, it is met with in diseased conditions which have no reference whatever to lead, the sign is thus to some extent shorn of much of its value." Russell (39), in one hundred consecutive examinations of persons receiving compensation for lead poisoning in the Stoke-on-Trent area, found stippled cells in only seventy-three cases.

Other workers on the subject maintain that basophilia is one of the first diagnostic signs of lead poisoning, and state that it is present in workmen who have not yet begun to complain of symptoms of plumbism. Schonfield (40) regards a negative basophilia as most important, for he makes use of the fact to encourage the men that they are not suffering from lead poisoning. Again, Schmidt (41) says that if stippled cells are present to the extent of one hundred per million red cells, upon this circumstance alone, a diagnosis of plumbism may be made.

The literature on the subject therefore appears to state that while punctate basophilia is a sign of great importance in the early diagnosis of lead poisoning, it is by no means pathognomonic of that condition. I believe that where stippling occurs one must suspect plumbism as being the cause until investigation can rule it out. The other conditions

giving rise to stippling should occasion no difficulty in diagnosis. My experience with stippling in conditions other than lead poisoning is very limited. Two cases can be recalled. The first was that of a woman suffering from pernicious anaemia. When seen she presented the usual colour of that condition, did not show any sign of having lost weight, described the usual symptoms and gave the usual history. The diagnosis seemed easy. But if one had tried to base one's diagnosis on the appearance of a blood film alone, then it would have been difficult to say whether the film was from pernicious anaemia or from lead poisoning, because of the very large number of red cells which showed stippling. But apart from stippling, the appearance of the film did not leave any doubt as to the diagnosis. The red cells were obviously larger than normal, while poikilocytosis and anisocytosis were very marked. The second case was that of a man suffering from an annular carcinoma of the transverse colon. No tumour of any kind was to be felt on palpation, the abdominal muscles being kept rather rigid. The man was anaemic looking, had been losing weight, and was suffering from colic, constipation and vomiting. Lead colic had to be thought of in the diagnosis, and a blood film was examined. A very careful examination of almost the whole film showed only the presence of four cells with punctate basophilia. The stippling appeared very indistinctly, and was only discernable under the highest power of the microscope, quite different to the coarse stippling of plumbism which can be easily seen under an oil immersion lens with a XIO eyepiece.

If, as maintained by Schmidt (41), the presence of one hundred cells per million red cells, indicates undoubted lead poisoning, then the cases I have presented in this Thesis are undoubtedly cases of lead poisoning. It must be remembered

that the mere fact of stippling being present does not of itself signify plumbism. The case of pernicious anaemia already described showed on an average two stippled cells in every field examined, using an oil-immersion lens with an X6 eyepiece. This far exceeds one hundred per million red cells.

In this investigation, the presence of stippling played a very important part. When it was decided to investigate the incidence of lead poisoning among my patients using Scout Moor water, every patient who came to the consulting room from the suspected area, irrespective of his reason for attending, had a blood film examined for the presence of stippling. If this was found then such investigations as were possible were carried out until the diagnosis of plumbism was confirmed or disproved. From the results collected to date, I am convinced that punctate basophilia is a valuable diagnostic sign. I have examined blood films from fortyone consecutive cases coming from the suspected area, and in forty of these, punctate basophilia has been found. In the exception, the tap water was examined, but no lead was to be found. It appears that this method is in use in Leipzig for the early detection of lead poisoning, and that, if three hundred stippled cells are present per million red cells, the individual is suspended work and given treatment.

Summary.

(1) In this Thesis, it has been shown that one of the districts of Haslingden is receiving a soft moorland water, this water being acid in reaction and known to have an action on lead. The water receives no treatment of any kind

being delivered to the consumer.

(2) Examination of a series of the tap waters concerned show that these contain lead in comparatively large quantities, and so prove that the cases described are definitely exposed to the action of lead.

(3) A series of cases suffering from the effects of chronic lead poisoning have been described, and the general symptoms of plumbism discussed.

(4) Controversial points have been discussed in full, and the importance of punctate basophilia in the early diagnosis of plumbism emphasized.

Methods of Examination of Blood and Urine.

Blood.

Haemoglobin. This was estimated by Sahli's Haemometer. The tube was filled to the mark 10 with N/10 HCl, the blood added to this, and the mixture left for one minute. Distilled water was then added until the colour compared with that in the standard tube.

Red cell count. A Thoma counting chamber was used with Toisson's diluting fluid. In each count 64 small squares were scrutinised, three separate counts were made, and the average taken for the calculation. In every case the dilution of blood was 1 in 200.

White cell count. Here the diluting fluid used was 3% acetic acid. The dilution used was 1 in 20. Three separate counts of 256 small squares were made, and the average taken for the calculation.

Blood films. All the films examined were stained by Pappenheim's "panoptic method" described by Piney (17). In this method, air dried films are kept for about 24 hours before staining. The film is covered with Jenner's stain, which is kept on for 4 minutes. An equal amount of distilled water is then added, and the film left for one minute longer. The diluted stain is now poured off, and, without washing, the film is covered with dilute Giemsa stain (one drop of Giemsa stain to one cc. of distilled water). This is allowed to act for seven minutes, then poured off and the film washed in distilled water for 30 seconds. Drying is

effected at room temperature by waving the film about. It is not necessary to mount the film. All the films were examined with an oil-immersion lens, using a X 6 eyepiece.

Differential count. This was carried out with the use of oil-immersion lens, using a X6 eyepiece. Each count was carried out in the same way, starting at the top left hand side of the film and counting half way across the film and then back to the edge again, using a movable stage. In this way 250 white cells were counted, and the percentages calculated.

Stippled cell count. A diaphragm with a minute central hole was inserted into the X6 eyepiece. The hole was just large enough to allow a field containing about ten red cells to be seen. The film was moved as in the differential count, and three thousand red cells were counted. The result was expressed as per million red cells.

Urine. The ordinary routine tests were carried out in the usual way. In the examination for the presence of lead, von Jacksh's method, as described by Glaister, was used. The test is carried out as follows - a strip of bright lead-free magnesium ribbon is placed in a urine jar containing about 10 oz. of urine. Ammonium oxalate is added in the proportion of 1 gramme to 150 cc. urine, and the whole left standing until a deposit forms on the ribbon. This usually takes two to three days.

The ribbon is then washed in distilled water, gently dried, and then held over a warm porcelain dish in which one crystal of pure iodine is placed. The development of a yellow colour indicates the formation of lead iodine. The only other metal which will give a yellow colour is cadmium, and this is not likely to be present in the urine. The lead iodide is dissolved in dilute nitric acid, and confirmatory tests for lead applied.

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